Assessment of Soft Tissue Facial Profile, Nasal Airway Morphology and Dental Arch Features in Adult Malay Obstructive Sleep Apnea Patients using Geometric Morphometric Analysis

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We live in a sea of apnea; the sleep centre can be a life saver

Lyle D. Victor

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LIST OF ABBREVIATIONS

Abbreviation	Definition
2D	Two-dimensional
3D	Three-dimensional
AASM	American Academy of Sleep Medicine
AHI	Apnea-hypopnea index
AR	Acoustic rhinometry
ASDA	American Sleep Disorders Association
BMI	Body mass index
CI	Confidence interval
cm	Centimeter
cm^2	Centimeter square
cm^3	Centimeter cube
CPAP	Continuous positive airway pressure
CSA	Cross sectional area
CT	Computerized tomography
dB-SPL	Decibel-sound pressure level
ECG	Electrocardiography
EDS	Excessive daytime sleepiness
EEG	Electroencephalogram
EFF	Elliptical fourier functions
EMG	Electromyography

ENT	Ear, nose and throat
EOG	Electrooculogram
FEA	Finite element analysis
FEM	Finite element morphometry
FESA	Finite element scaling analysis
GG	Genioglossus dilator muscles
HUSM	Hospital Universiti Sains Malaysia
ICD	Inter-canine distance
ID	Identity number
IMD	Inter-molar distance
IP1D	First inter-premolar distance
IP2D	Second inter-premolar distance
kg	Kilogram
m	Meter
m^2	Meter square
MAA	Medial axis analysis
MCA	Minimal cross-sectional area
MCA1	Minimal cross-sectional area 1
MCA2	Minimal cross-sectional area 2
mm	Milimeter
MM	Morphometric model
mm^2	Milimeter square
MMP	Mallampati grade
MRI	Magnetic resonance imaging

MSLT	Multiple sleep latency test
MWT	Maintenance of wakefulness test
n	Sample size
NC	Neck circumference
NPV	Negative predictive value
ORL-HNS	Otorhinolaryngology-Head and Neck Surgery
OSA	Obstructive sleep apnea
OSAHS	Obstructive sleep apnea – hypopnea syndrome
OSAS	Obstructive sleep apnea syndrome
PCA	Principal component analysis
PDS	Portable device system
PPV	Positive predictive value
PSG	Polysomnography
RDI	Respiratory disturbance Index
SAHS	Sleep apnea / hypopnea syndrome
SD	Standard deviation
SDB	Sleep disorder breathing
SE	Standard error
SNAP	Sleep apnea snoring analysis product
SpO_2	Hemoglobin oxygen saturation
SPSS	Statistical Package for Social Sciences
TP	Tensor palatini dilator muscles
TPS	Thin plate spline analysis
UARS	Upper airway resistance syndrome

UPPP	Uvulopalatopharyngoplasty
URTI	Upper respiratory tract infections
USM	Universiti Sains Malaysia
WHO	Word Health Organization

Penilaian Profil Tisu Muka, Morfologi Salur Udara Hidung dan Ciri-Ciri Rahang Gigi di Kalangan Pesakit Melayu Dewasa Bermasalah Tidur Apnea Obstruktif Menggunakan Analisis Morfometrik Geometrik

ABSTRAK

Masalah tidur apnea obstruktif (OSA) telah dikenal pasti sebagai satu masalah yang memberi impak kepada masyarakat setanding dengan masalah merokok. Namun begitu, OSA masih belum dapat dikenal pasti dan tidak didiagnos dengan meluas. Tujuan kajian ini ialah untuk mengenal pasti lokasi dan kuantiti perbezaan profil tisu muka, morfologi salur udara hidung dan ciri-ciri rahang gigi di kalangan Melayu dewasa yang bermasalah dan tidak bermasalah OSA menggunakan analisis morfometrik geometrik. Setelah mendapat keizinan, 120 orang Melayu dewasa berumur 18-65 tahun (min ± SD, 33.2 ±13.31) telah dibahagikan kepada dua kumpulan yang mempunyai 60 orang setiap kumpulan. Kedua-dua kumpulan OSA dan kawalan telah menjalani pemeriksaan klinikal dan ujian polisomnografi rangkaian terhad. Hanya 108 subjek (54 setiap kumpulan) berjaya menjalani pengimejan tisu muka, pengukuran rinometri akustik (AR) dan impresi rahang gigi atas dan bawah. Sembilan penanda tisu muka dan 25 penanda homologus pada model rahang gigi atas dan bawah telah didigitasi menggunakan perisian MorphoStudio untuk mendapatkan koordinasi x, y, z. *Minimal cross section* 1 (MCA1) dan *minimal cross sectional* 2 (MCA2) didapati daripada AR dan, min kedua-dua kumpulan OSA dan kawalan dihitung, seterusnya ujian-t dan analisis morfometrik geometrik dilakukan. Keputusan menunjukkan min indeks jisim badan didapati lebih signifikan untuk kumpulan OSA (33.2kg/m^2 ± 6.5) berbanding dengan kumpulan kawalan (22.7 kg/m^2 ± 3.5, $p < 0.001$).

Min saiz leher didapati lebih besar untuk kumpulan OSA (43.6cm ± 6.02) berbanding dengan kumpulan kawalan (22 ± 3.52, $p < 0.001$). Dengan menggunakan analisis morfometrik geometrik, terdapat perbezaan signifikan pada dua kumpulan tersebut. Perbezaan tisu muka didapati terletak terutamanya di bahagian *bucco-submandibular* muka, dengan jarak antara penanda menunjukkan pertambahan pada saiz iaitu 7-22% ($p < 0.05$) untuk kumpulan OSA. Untuk morfologi salur udara hidung, min MCA1 and MCA2 pada graf AR didapati kecil secara signifikan untuk kumpulan OSA berbanding dengan kumpulan kawalan ($p < 0.001$). Analisis morfometrik geometrik ke atas data AR mendapati terdapat perbezaan signifikan pada salur udara hidung di antara kedua-dua kumpulan. Min salur udara hidung kumpulan OSA lebih sempit secara signifikan dengan pengurangan saiz (≈10-22%) didapati di bahagian *nasal valve / head inferior turbinate*. Untuk ciri-ciri rahang gigi, min morfologi rahang gigi atas dan bawah OSA mempunyai kelebaran yang lebih sempit secara signifikan dengan pertambahan panjang pada rahang gigi atas dan bawah berbanding dengan kumpulan kawalan ($p < 0.05$). Min konfugurasi rahang gigi atas ialah 7-11% lebih sempit di aras *transverse* di bahagian insisor and kanin berbanding konfigurasi kawalan, dan analisis antara penanda mengesahkan keputusan ini. Untuk rahang gigi bawah min konfigurasi OSA ialah 10-11% lebih sempit di aras *antero-posterior* di bahagian premolar dan molar. Kesimpulannya, jelas sekali terdapat perbezaan yang nyata pada profil tisu muka, morfologi salur udara hidung dan ciri-ciri rahang gigi bila dibandingkan antara pesakit OSA dengan kawalan, dan obesiti menjadi faktor risiko tambahan dalam kumpulan pesakit Melayu tersebut.

Perbezaan ini perlu dikenal pasti memandangkan ianya dapat membantu pemahaman kita mengenai asas etiologi masalah OSA, membantu suasana diagnostik yang terhad dan memberi maklumat bermakna semasa saringan untuk mengesan pesakit yang tidak didiagnos bermasalah OSA.

Assessment of Soft Tissue Facial Profile, Nasal Airway Morphology and Dental Arch Features in Adult Malay Obstructive Sleep Apnea Patients Using Geometric Morphometric Analysis

ABSTRACT

Obstructive sleep apnea (OSA) has been described as a public health problem comparable to smoking in its impacts upon society. Despite that claim, OSA is still widely unidentified and undiagnosed. The objectives of this study were to localize and quantify the differences in facial soft tissue profile, nasal airway morphology and dental arch features in adults Malay with and without OSA using geometric morphometric analysis. After obtaining appropriate consent, 120 adult Malays aged 18-65 years (mean ± SD, 33.2 ± 13.31) were divided into two groups of 60. Both OSA and control groups undergone clinical examination and limited channel polysomnography. 108 subjects (54 in each group) were able to complete facial soft tissue imaging, acoustic rhinometry (AR) measurements, and upper and lower dental impression. Nine facial soft tissue and 25 upper and lower study models homologous landmarks were digitized using MorphoStudio software to obtain the x, y, z coordinates. The minimal cross section 1(MCA1) and minimal cross sectional 2 (MCA2) were also obtained from AR. The mean OSA and control were computed, and subjected to t-test and geometric morphometric analysis. The result shows that the mean body mass index was found to be significantly greater for the OSA group (33.2kg/m^2 ± 6.5) when compared to the control group (22.7 kg/m^2 ± 3.5 $p < 0.001$). The mean neck size was also greater for the OSA group (43.6cm ± 6.02) compared to the control group (22.7cm ± 3.52, $p < 0.001$).

Using geometric morphometric analysis, significant differences were found in facial soft tissue profile between the two groups. These differences were localized in the bucco-submandibular regions of the face predominantly, with inter-landmark distances indicating an increase in size of 7-22% in OSA groups ($p < 0.05$). For nasal airway morphology, the mean MCA1 and MCA2 on the AR graph were found to be significantly smaller in the OSA group than control group ($p < 0.001$). Using geometric morphometric analysis on AR data, significant differences were found in nasal airway morphology between the two groups. Specifically, the mean nasal airway of OSA groups were significantly narrower in OSA groups with decreased in size (≈10-22%) appears in nasal valve / head of inferior turbinate area predominantly. For dental arch features, the mean upper and lower OSA dental arch morphologies were significantly narrower in widths with an increase in upper and lower dental arch length when compared with control subjects ($p < 0.05$). Specifically, the mean OSA configuration of the upper arch was 7-11% narrower in the transverse plane in the incisor and canine regions compared to the control configuration, and inter-landmark analysis confirmed this finding. For the lower arch, the mean OSA configuration was 10-11% narrower in the premolar and molar regions. In conclusion, there were clearly definable differences in the facial soft tissues profile, nasal airway morphology and dental arch features when comparing patients with OSA to controls, with obesity acting as an additional risk factor in this particular group of Malay patients. These differences need to be recognized since they can improve our understanding of etiological basis of OSA disorder, facilitate the limited availability of diagnostic setup, and provide valuable screening information in the identification of patients with undiagnosed OSA.

CHAPTER 1

INTRODUCTION

1.1 Background

It is striking that a condition as common as obstructive sleep apnea (OSA) has only come to the forefront in the last 30 years (Caples et al., 2005). Indeed, much of what we have learned about sleep apnea has occurred in the very recent past. The first description of OSA that identified the upper airway obstruction as the major pathogenic mechanism was in 1965 (Pack, 2006).

In late 19th century, there were clinical descriptions of cases of obesity with extreme excessive sleepiness. The physicians recognized that these cases were similar to the description of the fat boy in the Pickwick Papers. This led, in time, to the use of the term "Pickwickian syndrome" to describe the combination of obesity and noticeable excessive sleepiness (Dement, 1998). However, recently, the term Pickwickian syndrome has a more precise meaning and restricted to those obese individuals who further have hypoventilation during wakefulness (Pack, 2006).

Dement (1998) reported that the first tracheotomy with the intention of bypassing airway obstruction that occurred during sleep was carried out by Kuhlo and his groups in 1969.

Subsequently, the association between periodic cessation during sleep and fluctuations in heart rate were revealed in 1971; however, the obstruction of the upper airway was not yet recognized as the cause for the cessation of respiration (Pack, 2006).

Since then, progress has been remarkable as high prevalence of OSA was revealed by strong epidemiological study (Young et al., 1993). Realizing that OSA was far from being rare, OSA was then recognized as a major public health issue (Phillipson, 1993).

On the other hand, along with an increasing scientific approach to OSA, its precise definition has become somewhat controversy. Conventionally, apnea means 'without breath' in Greek word (Chokroverty, 2001).

To compound the matter even further, the definition of apnea differs among sleep laboratories and in medical literature. For example, Caples et al. (2005) defined apnea as nearly complete cessation of airflow associated with oxygen desaturation or an arousal from sleep. Qureshi and Ballard (2003) described OSA as repeated complete or partial upper airway obstruction during sleep, causing cessation of breathing (apnea) or reduction of airflow (hypopneas) despite persistent respiratory effort. In adult, 30% to 50% reduction in airflow for at least 10 second is characteristic of OSA patients (Attarian and Sabri, 2002).

1.2. Prevalence of Obstructive Sleep Apnea

Understanding disease prevalence, that is, the ratio of a population with the condition, is critical to anticipate health care needs and designating proper resources (Young et al., 2002). In addition, comparisons of prevalence by demographic factors may give evidences to etiological factors and identify high-risk groups (Young et al., 1993). Young et al. (2002) noted that disagreements in definitions of disease and sampling biases contribute to the wide range of prevalence of OSA noted in the literature.

However, previous studies of OSA prevalence have taken some of these concerns into account by approximately adjusting the differences in definitions or by comparing results from studies with similar study designs. For example, Davies and Stradling (1996) estimated that 1% to 5% of adult men have obstructive sleep apnea syndrome (OSAS) in Western populations.

Data from Wisconsin Sleep Cohort study suggested that the prevalence of OSA among middle-aged adults women and men were 9% and 24% respectively (regardless presence of symptom) while the prevalence of OSAS (OSA plus presence of excessive daytime sleepiness) was 2% in women and 4% in men (Young et al., 1993).

Other studies who used similar in-laboratory diagnostic criteria and sampling methods estimated that one out of every five adults has at least mild OSA and one of every 15 has at least moderate OSA (Bixler et al., 1998; Bixler et al., 2001).

However, most of these studies are Western studies performed in predominantly white populations and may not be applicable to other racial groups. Therefore, the prevalence of OSAS and its symptoms (e.g snoring) among Asian populations were getting worldwide recognition. For instance, the prevalence of snoring in Singaporean population between different ethnic group were reported by Ng et al. (1998); as lowest in Chinese subjects (6.2%), highest in Indians (10.9%) while Malay subject had a prevalence of 8.1%.

Other study has revealed that the prevalence of snoring in Chinese study subject was at 23% (Ip et al., 2001). Hasnah (2005) examined army personnel based in Kelantan and suggested that the prevalence of snoring among the study subject was at 28.2%. Moreover, in the same study 6.5% reported that they had breathing pauses observed by others at least 3 to 4 times a week (Hasnah, 2005). Currently, the prevalence of snoring among Malaysian children aged 7 to 15 years were reported to be 14.51% (Banabilh et al., 2007a).

On the other hand, Ip et al. (2001) reported the first estimates of OSA prevalence in an Asian population, using two-stage sampling methodology and polysomnography (PSG). From a survey sample of 784 Hong Kong men, between 30 to 60 years of age, of these 153 completed PSG studies, estimated that 4% is the prevalence of OSA in men (Ip et al., 2001). Similarly, preliminary data from a similar study of Chinese women in Hong Kong indicated a conservative estimate of OSAS prevalence of 2% in women (Ip et al., 2004).

Pasha and Khan (2003) used questionnaire survey in Pakistani adults and suggested that 6% of male and 5% of the female participants in their study had symptoms of sleep apnea.

Another Asian study conducted in Indian population estimated the prevalence of OSA among middle-aged urban Indian men to be at 19.5% and when combined with excessive daytime sleepiness (EDS), the prevalence was 7.5% (Udwadia et al., 2004). Unfortunately, Malay local data are scanty. A study among the staff members of Hospital Universiti Sains Malaysia (HUSM) suggested that the prevalence of OSAS is 4.0% with 19.8% of subject admitted of being heavy snorers (Kumar, 2000).

1.3 Classification of Sleep Apnea

1.3.1 Obstructive Sleep Apnea

Among all sleep apnea types, obstructive sleep apnea (OSA) and obstructive sleep apnea syndrome (OSAS) garners most of the attention in the literature. Therefore, it is important to distinguish between OSA and the OSAS. Thus, OSAS is a common clinical aspect of sleep disorder, in which daytime sleepiness or related problem in daytime function are recognized (Gibson, 2004).

The obstructive sleep apnea syndrome is commonly associated with loud snoring; apneic events such as choking and gasping during sleep (George et al., 2003). Indeed, the only two symptoms that make OSA patients attend the clinic are loud snoring and EDS (Dobbin and Strollo, 2002).

Obstructive sleep apnea syndrome is often associated with significant morbidity, largely due to impaired daytime function, with excessive daytime sleepiness and consequent increased risk of accidents and cardiovascular complications (Dobbin and Strollo, 2002).

1.3.2 Central Sleep Apnea

The less common form of sleep apnea is called central sleep apnea; it takes place when brain fails to send appropriate signals to the breathing muscles to initiate respiration, which lead to reduction or absence of respiratory effort (Flemons, 2002).

1.3.3 Mixed Sleep Apnea

The combination of central and obstructive may lead to mixed type of sleep apnea with features suggesting initially a central and then obstructive event during sleep (Gibson, 2004).

1.3.4 Sleep Hypopnea

Sleep hypopnea definitions also vary from one laboratory to another. For example, Pack (1994) reported that hypopnea occurs when the airflow decremented by 35% to 50% for 10 seconds or more associated with a 4% fall in oxygen saturation and/or terminated by an arousal. Hui et al. (2000) stated that any reduction in amplitude of airflow of $\geq$ 50% of the baseline measurement that last for 10 seconds called hypopnea.

1.4 Obstructive Sleep Apnea and Hypopnea Indices

Assessments of OSA severity were also getting worldwide attention. These assessments are mainly based on apnea-hypopnea index (AHI), which is defined as number of apnea plus hypopnea per hour of sleep (Flemons et al., 2003).

The apnea-hypopnea index has been used to classify patients as either having OSA or being normal (AHI < 5 events per hour of sleep), as well as to classify the severity of OSA. The American Academy of Sleep Medicine (AASM,1999) classified OSA severity according to AHI as mild sleep apnea (AHI 5 to 15 events per hour of sleep); moderate sleep apnea (AHI 15 to 30 events per hour of sleep); severe sleep apnea (AHI > 30 events per hour of sleep).

Even though AHI has proven to be superior in assessing the extensive effect of OSA, however, it may be unsuitable for characterizing OSA in specific subsets of patients (Hosselet et al., 2001). This is because; AHI measures the frequency of disordered breathing events but does not quantify other processes that may be involved in the pathophysiology of OSA, such as the degree of oxygen desaturation (Caples et al., 2005).

Furthermore, the total number of arousals, some of which may occur in the absence of frank breathing abnormalities, may be a superior marker of sleep fragmentation than the AHI and may better explain daytime sleepiness (Caples et al., 2005). However, the AHI remains in general use and the recommended diagnostic criteria for OSA (AASM, 1999).

1.5 Upper Airway Resistances Syndrome

Guilleminault at Stanford University was the first to introduce upper airway resistance syndrome (UARS) (Guilleminault et al., 1992). The main features of UARS are chronic daytime sleepiness in the absence of actual apneas or hypopneas. It is often associated with snoring and frequent arousals with an only slightly abnormal breathing pattern (Guilleminault et al., 1993).

In addition to frequent snoring, restlessness during sleep and sweating, other characteristics of UARS included changes in appetite, poor performance in school and problems with behavior in children (Downey et al., 1993).

Initial studies of UARS by Guilleminault et al. (1992) showed that it only strike men but afterward it was recognized that the syndrome was also present in women, with a roughly equal gender distribution (Strollo and Sanders, 1993).

Woodson (1996) reported that UARS patients are typically non-obese with a mean body mass index (BMI) of < 25 kg/m^2 and frequently younger than OSAS patients. In addition, low soft palates, long uvula, increased overbite and high narrow hard palate are also recognized in this syndrome (Exar and Collop, 1999). However, combination of these features with EDS, hypertension and snoring may make these patients impossible to be differentiated clinically from OSAS patients in the absence of PSG (Silverberg and Oksenberg, 1997).

1.6 Risk Factors Associated with Obstructive Sleep Apnea

1.6.1 Gender and Age

Gender differences were frequently reported as being risk factors associated with OSA (Ryan and Bradley, 2005). In the past, OSA was mainly identified as a disease of men (Resta et al., 2004). This was because early epidemiological studies on OSA included only men and most patients referred to sleep clinics with sleep disorder breathing (SDB) were men. For the first time, Young et al. (1993) included women in a study examining the prevalence of OSA in Wisconsin Sleep Cohort Study.

In Wisconsin Sleep Cohort study, the prevalence of OSA in men 24% was almost three times higher than in women 9% (Young et al., 1993). These findings suggest that the presence of OSA in women may be largely underestimated in clinical practice, possibly because OSA has different clinical features and characteristics in women with respect to men (Resta et al., 2004).

Despite the fact that women with OSA tend to be more obese and have smaller upper airway size than men, OSA is still more common in men than women (Young et al., 1993). Pillar et al. (2000) reported that men demonstrated more collapsibility of the upper airway during sleep than women when exposed to an external inspiratory load. Similarly, pharyngeal airway length, soft palate area and pharyngeal volume increase were reported in men more than women (Malhotra et al., 2002). However, Ryan and Bradley (2005) indicated that with normal aging the upper airway becomes smaller and more collapsible.

On the other hand, not only sleep disordered breathing (SDB) are more common in men its severity also depending on the gender. Men have more severe sleep apnea than women do, although this difference becomes less significant for postmenopausal women (Bixler et al., 2001).

The reasons for the gender differences in the prevalence and severity of sleep apnea are multifactorial. Millman et al. (1995) suggested that body fat distribution was the most important factor in developing more severe form of sleep apnea in men.

Pillar et al. (2000) and Zhou et al. (2000) concluded that abnormalities in upper airway mechanics, differences in breathing control and upper airway dimensions were accountable for gender differences.

The differences in bony configuration, fat deposition and soft tissue structures make man upper airway more susceptible to collapse (Malhotra et al., 2002). In contrast, Rowley et al. (2001) measured upper airway resistance and critical closing pressure in normal men and women during sleep and found no gender-related differences.

The prevalence and severity of OSA between men and women can also vary according to age. Both the prevalence and the severity of OSA were higher in men than in women of the same age range (< 55 years) (Resta et al., 2004). Alternatively, in subjects more than 55 years both the prevalence and the severity of OSA were completely overlapping (Resta et al., 2004).

On the other hand, the associations of gender, sleep apnea and pharyngeal properties were also reported in some studies with conflicting results. For example, Trinder et al. (1997) found similar pharyngeal resistance during sleep in healthy men and women, but men show greater increments in upper airway resistance than women. Other investigators failed to find consistent differences in pharyngeal structure or function during sleep (Thurnheer et al., 2001; Rowley et al., 2001).

The upper airway anatomy differences between men and women were also investigated. Mohsenin (2001) found that men with sleep apnea had larger pharyngeal cross-sectional area than women using acoustic reflection measurements, but the correlation between pharyngeal area and apnea severity was inconsistent.

However, cephalometric measurements do not demonstrate consistent differences in pharyngeal area between men and women, with some investigators showed relatively minor changes in certain ethnic groups of men versus women (Lowe et al., 1996).

The pattern of fat deposition was reported to be different in apneic men and women. As women become obese, more fat is deposited over the lower body as compared to the neck. By the time, an apneic woman achieves the same AHI and neck circumstances (NC) as a man, her BMI become higher than that of man (Dancey et al., 2003).

In this regards, the classic symptoms of OSA (loud snoring, excessive daytime sleepiness, bad memory, choking) were similar by men and women despite higher respiratory disturbances index (RDI) in men (Resta et al., 2003). Pillar and Lavie (1998) noted that women demonstrate different typical symptoms, such as frequent awakenings, headache and depression, regardless of the severity of OSA compared to men.

In a previous study, Guilleminault et al. (1995b) suggested specific craniofacial morphometric features of women with mild sleep apnea. These features included a triangular chin, increase in the over jet, a narrow hard palate and Class II malocclusion.

However, these morphometric characteristic of men and women need to be further studied since such characteristic may be useful in understanding the pathogenesis of OSA. Nevertheless, Schwab (1999) concluded that in addition to gender, there must be other important factors that affect upper airway caliber and increase the risk for sleep apnea.

1.6.2 Obesity

Early studies of sleep apnea emphasized the importance of obesity as a significant determinant of SDB. For instance, The Wisconsin Sleep Study Cohort reported that obesity is considered as an increase risk for sleep apnea in adults of both sexes (Young et al., 2002).

In Asian men and despite the presence of severe illness, OSA has been found more frequently in non-obese patients when compared with white OSA male patients (Li et al., 2000). Kubota et al. (2005) found that obesity and dolico facial pattern were the most significant risk factors in Japanese men. Ono et al. (1996) reported that obesity significantly correlated with OSA severity.

The etiology and craniofacial features of OSA in obese patients may be differing from that in non-obese patients (Sakakibara et al., 1999). For instance, Yu et al. (2003) suggested that narrowing of the bony oropharynx, an enlarged soft palate and shifting of the tongue mass to the hypo pharyngeal space may combine to play an important role in the development of OSA in non obese patients.

In obese patients, more extensive and severe enlargement of soft tissues were found such as an enlarged soft palate, an anteriorly positioned hyoid bone and a longer tongue (Ferguson et al., 1995).

Obesity is usually estimated by calculating the body mass index (BMI). The BMI calculated by measuring the weight of the patients in kilogram divided by height in meter square. However, having a high BMI is not an absolute precondition for having OSA. Patients can have OSA yet have very low BMI (Ferguson et al., 1995). Therefore, the combination of factors that includes both oropharyngeal anatomic abnormalities as well as the size of the patient might be more predictive of OSA than any single factor alone (Friedman et al., 1999).

Word Health Organization (WHO) classified BMI cut-off point as severe underweight (<16 kg/m^2), moderate under weight (16.0-16.9 kg/m^2), mild underweight (17.0-18.49 kg/m^2), normal weight (18.5-24.9 kg/m^2), over weight (≥25), pre-obese (25-29.9 kg/m^2) and obesity (≥30 kg/m^2) (WHO expert consultation, 2004).

However, for the Asian population WHO redefined the acceptable BMI range, because many cardiovascular disease, hypertension and metabolic syndrome have been shown to occur at lower levels of BMI in these ethnic groups. Therefore, WHO suggested new cut-off point for the Asian population.

The new cut-off point for observed risk varies from 22 kg/m^2 to 25 kg/m^2 in different Asian populations; for high risk it varies from 26 kg/m^2 to 31 kg/m^2 (WHO expert consultation, 2004). Moreover, the consultation also reported that there was no clear single cut-off point for all Asians for overweight or obesity (WHO expert consultation, 2004).

In addition to obesity, neck size is also considered as one of the most important physical characteristic of patients with sleep apnea. Mortimore et al. (1998) concluded that non-obese patients with OSA have increased fat deposition adjacent to the upper airway compared with control subjects.

Obese patients with sleep apnea had 44% more total body fat and 67% more total neck fat than did control subjects (Whittle et al., 1999). The same group of researchers noted also that the necks of men contain a higher proportion of fat than their bodies as a whole, while the reverse is true of women matched for BMI.

1.6.3 Nasal Obstruction

Nasal obstruction may contribute to the development of OSA (Houser et al., 2002). However, this remains a point of controversy. Some authors claimed it might cause frank OSA, whereas others minimize the role of nasal obstruction (Scharf and Cohen, 1998).

A deviated nasal septum or allergic or non-allergic rhinitis can cause nasal obstruction. Indeed, SDB was noted when nasal obstruction was induced (Tanaka and Honda, 1989).

Morris et al. (2005) hypothesized four proposed mechanisms by which nasal obstruction may lead to OSA. The first hypothesis stated that, an increased in nasal airway resistance elevate respiratory effort, which increases intra-pharyngeal pressure, crushing pharyngeal dilator muscles and leading to upper airway collapse.

The second hypothesis suggested that nasal obstruction predisposes the individual to mouth breathing, allowing the tongue and mandible to shift backward. Thus, increases airway narrowing and intra-luminal, negative pressure that lead to increased airway resistance, causing collapse.

The third hypothesis proposed that the nasal obstruction might lead to persistent snoring, which increases respiratory effort, predisposing to airway collapse.

The fourth theory suggested that nasal obstruction might activate the naso-pulmonary reflex, which leads to abnormal decrease in nasal trigeminal nerve stimulation followed by fall in pulmonary ventilation (Morris et al., 2005).

In patients who are overweight, nasal obstruction may play a relatively slight role compared with obstruction at other anatomic levels. In patients with low BMI, who likely have thinner necks and relatively normal upper airway anatomy, nasal obstruction may play a critical factor in upper-airway collapse (Morris et al., 2005).

1.6.4 Family History

Family history is regarded as an important risk factor for high AHI and associated symptoms, such as snoring, daytime sleepiness and apneas (Redline and Tishler, 2000).

The prevalence of OSA among first-degree OSA relatives varied from 21% to 84% (Redline et al., 1995; Guilleminault et al., 1995a). Mathur and Douglas (1995) reported that relatives of OSA patients have a more retroposed maxillae and mandibles, shorter mandibles, longer soft palates and wider uvula.

In addition, high and narrow hard palate associated with daytime symptoms of sleepiness has been demonstrated to be more common in first-degree relatives of patients with OSA (Guilleminault et al., 1995a).

1.6.5 Ethnicity

Ethnicity is considered as an important risk factor associated with the pathogenesis of OSA (Villaneuva et al., 2005). For instance, Asians have shorter maxillae and mandibles, smaller anterior-posterior facial dimensions and lower BMI than Caucasians (Lam et al., 2005).

In contrast, Cakirer et al. (2001) concluded that Caucasians tend to have increased soft tissue measurements of the tongue and soft palate compared to African–American subjects. Another study compared Caucasian, African–American and Hispanic subjects with moderate to severe OSA using cephalometric variables. Their results showed that significant bimaxillary prognathism among African–Americans and bimaxillary retropositioning among Hispanics relative to the other ethnic groups (Will et al., 1995).

Li et al. (2000) compared Far East Asian men (mainly Chinese) and Caucasians with OSA and reported that Asian men were found to be less obese for the same severity of OSA. Redline et al. (1997) suggested that African-American of less than 25 years of age were twice to have OSA of similar severity as Caucasian.

Ethnicity can also be a major detriment of OSA risk factors. For example, obesity was considered as the major risk factor in Caucasian populations. Whereas, craniofacial factors were more significant than obesity and soft tissue factors in Asians (Villaneuva et al., 2005).

1.6.6 Smoking and Alcohol

The effect of long-term use of alcohol and smoking on development of sleep apnea is not clear. Scanlan et al. (2000) supported the relationship between alcohol consumption and worsening of OSA. Alcohol increased the nasal resistance, acts as central depressant, and muscle relaxant. On the other hand, smoking may be a possible risk factor for SDB. Wetter and his colleagues (1994) found that heavy smokers (> 40 cigarettes per day) had a greatest risk for OSA with odds ratio of 6.7 for mild and 40.0 for severe OSA.

1.6.7 Genetic

Obstructive sleep apnea was recognized as genetically complex disease that results from various interacting genetic and environmental factors (Palmer and Redline 2003). Whitsett et al. (2004) noted a strong familial and genetic basis for not just obesity but also for other OSA related phenotypes such as neck circumference, waist/hip ratio, high-density lipoprotein cholesterol, inter-maxillary cranial length and posterior airway space. A whole genome analyses study indicated that there were both shared and unshared genetic determinants of AHI and BMI (Palmer et al., 2004). Many genes have been considered as intermediate phenotypes for OSA. For example, leptin, adenosine deaminase and melanocortin-4 receptor were consider as candidate genes for obesity (Bray and Bouchard, 1997). Thus, genetic approaches to OSA offer great potential to improve our understanding of the pathophysiology of this disorder (Palmer et al., 2003).

1.7 Consequences Effect of Obstructive Sleep Apnea

Many OSA patients report a long history of symptoms for many years. Kryger et al. (1996) reported that apnea patients are heavy users of health care resources, not only at the time of diagnosis, but also for years prior to diagnosis.

The significant reduction in resource utilization (physician claims and hospital stays) was associated with early diagnosis and treatment of apnea patients (Bahammam et al., 1999b). Smith et al. (2002) noted that apnea patients are more ill and obtain incorrect diagnoses than control subjects. The same groups of investigator concluded that apnea patients used medical resources at significantly higher rates than the control subjects group (Smith et al., 2002).

A survey of health care utilization among 181 OSA patients showed that OSA patients had already been heavy users of health services for several years and the estimated cost of this care was twice as much as that of average patients (Ronald et al., 1999).

Kapur et al. (1999) estimated that in USA, untreated sleep apnea might have additional medical costs of as much as $3.4 billion per annum. On top of that, the OSA patients might have a consequence of effect that varies from motor vehicle and occupational accidents to hypertension and cardiovascular morbidity.

1.7.1 Motor Vehicle and Occupational Accidents

Accidents related to falling asleep estimated to be as much as 16-20 % of all motor vehicle accidents (Horne and Reyner 1995). Habitual snorers with AHI < 5 had an odds ratio of 2.9 for multiple motor vehicle accidents compared with 7.3 in subjects with AHI > 15 (Young et al., 1997a).

Men reported with both snoring and EDS had a two-fold risk for occupational accidents. Landrigan et al. (2004) reported that medical doctors with more than 24 hours work shifts suffer from 35.9% more serious medical errors in intensive care units.

The medical practitioner who worked extended shifts (average 32 hours) had a 2.3 times greater chance of an automobile crash and a 5.9 times greater chance of a near-miss crash compared with interns who worked a shorter shift (Barger et al., 2005).

1.7.2 Hypertension and Cardiovascular Morbidity

There is a growing agreement that OSA is an important risk factor for hypertension independent of excess weight and other potentially confounding factors (Young et al., 2002) Hla et al. (1994) reported that 30 % to 45 % of patients with OSA have systemic hypertension.

Peppard et al. (2000) concluded that in patients with OSA, hypertension is considered as a powerful indirect risk factor for congestive heart failure. Lavie et al. (2000) found significant associations between OSA and increased blood pressure in large samples of sleep clinic patients.

Lindberg et al. (1999) reported that self-reporting history of snoring were associated with self-reporting history of hypertension.

However, many cross sectional study indicated that the relationship between OSA and hypertension take place in younger and less obese individual more often than older, heavier subjects (Young et al., 1997c; Bixler et al., 2000). In contrast, Nieto et al. (2000) reported that SDB were associated with hypertension in middle and elder age groups of different sex and ethnics' background.

Obstructive sleep apnea can also contribute to cardiovascular disorder and cerebrovascular morbidity and mortality. Caples et al. (2005) noted that at least 10% of patients with heart failure have clinically significant OSA. The mortality in sleep clinic patients revealed that OSA might lead to increased cardiovascular disorder mortality. For example, Peker et al. (2000) found that OSA increases the risk of mortality in Swedish patients. Similarly, the occurrence of stroke, myocardial infraction and death were associated with OSA incidence (Mooe et al., 2001).

1.8 Statement of the Problem

Published literature revealed that OSA patients are widely unrecognized and undiagnosed. The failure to recognize the syndrome is in part due to limited availability of diagnostic facilities which, make them a heavy users of health care resources, not only at the time of diagnosis, but also for years prior to diagnosis.

Moreover, the need for accurate, quantitative diagnostic criteria is further supported by the significant cost incurred with routine PSG. However, the lack of simple, non-invasive, repeatable method has been an obstacle for the early recognition of OSA patients.

In addition, there is little evidence regarding facial soft tissue, nasal airway morphology and dental arch in Asian populations. Therefore, this study had investigated the diagnostic morphological features in adults with and without OSA using geometric morphometric analysis. Thus, could facilitate the early recognition of the syndrome and support the available diagnostic setup.

1.9 Objectives and Hypothesis

1.9.1 General Objectives

The general aim of this study was to investigate the diagnostic morphological features in adults with and without obstructive sleep apnea using geometric morphometric analysis.

1.9.2 Specific Objectives

I. To localize and quantify geometric morphometric differences in facial soft tissue profile among obstructive sleep apnea patients and control subjects

II. To localize and quantify geometric morphometric differences in nasal airway morphology in patients with obstructive sleep apnea and control subjects

III. To localize and quantify geometric morphometric differences of dental arch features in patients with obstructive sleep apnea and control subjects

1.9.3 Research Hypotheses

1. There is a difference in facial soft tissue profile in adults with and without obstructive sleep apnea
2. There is a difference in nasal airway morphology in adults with and without obstructive sleep apnea
3. There is a difference in dental arch features in adult with and without obstructive sleep apnea.